REMARKS

This application has been subjected to extensive prosecution and Applicants have restricted the claimed subject matter in an effort to reduce the issues and place the application in early condition for allowance. The present application has been restricted to the subject matter of claim 14 and claims dependent thereon. All of the claims have been canceled from the application without prejudice or disclaimer and subject to the right to file a further continuation thereof. Claim 14 was dependent on claim 11 which was dependent on claim 10. Thus, new claim 35 is a combination of claims 10, 11 and 14. Claims 12 and 13 have been rewritten as new claims 36 and 37. The claims now remaining in the application are claims 35-37.

Applicants most respectfully submit that all claims now pending in the instant application are in full compliance with the requirements set forth in 35 U.S.C. §112 and are patentable over the references of record

Applicants have carefully considered all of the rejections of the claims. There are only two rejections of claim 14, one of the grounds of obviousness under 35 USC 103(a) and the other on the grounds of provisional obviousness-type double patenting. The rejections of claims 10-13 have been obviated by the amendments to the claims, restricting the claim subject matter to that of claim 14. Accordingly, it is most respectfully requested that these rejections be withdrawn.

Applicants most respectfully submit that the individually detachable piezoelectric crystal microbalance flow-through cells recited in claim 35 are depicted most clearly in Figures 2 and 3 of the instant application. The flow-through cells 10 have a first half 14 and a second half 16 that combine to form a housing 12 that houses censor crystal 50. As shown in Figure 8, the flow-through cells 10 are connected to the rack 112, and more specifically, are inserted into the cell connector receptors 118. What is especially notable about the flow-through cells is they each form their own individual housing that is separate and distinct from other flow-through cells and that each flow-through cell is therefore individually detachable from its cell connector receptor. As explained in further detail throughout the specification, this allows for the replacement of any flow-through cell without requiring removal of other flow-through cells or disassembly of the

entire multiple piezoelectric crystal microbalance device. This feature is not suggested in the prior art applied in the rejection and would not be obvious to one of ordinary skill in the art.

The rejection of claim 14 under 35 U.S.C. §103(a) as being unpatentable over Karube et al. (USP 4,789,804, Dec. 6, 1988) (hereinafter "Karube") in view of Gardhagen et al. (USP 6,192,766 B1, Feb. 27, 2001) (hereinafter "Gardhagen"), Thorne (USP 4,154,795, May 15, 1979), constructing a formerly integral structure in various elements involves only routine skill in the art, and Takeuchi et al. (USP 6,326,563, filed Sept. 22, 1999) (hereinafter "Takeuchi") as applied to claim 11 above, and further in view of Ricchio et al. (USP 5,130,095, July 14, 1992) (hereinafter "Ricchio") has been carefully considered but is most respectfully traversed.

It is urged in the Official Action that Karube in view of Gardhagen, Thorne, and Takeuchi teaches the multiple piezoelectric crystal microbalance devices as set forth above. However, Karube in view of Gardhagen, Thorne, and Takeuchi fails to teach a multiple piezoelectric crystal microbalance device, further comprising grounding means for electrical grounding of the flow solution and the test solution aliquot to the cell compartment of each of the flow-through cell. It is then asserted that Ricchio teaches a flow cell having a solution grounding means on the inlet line for the sample adjacent to the entrance to the flow cell of fluid thereby minimizing electronic noise (see entire document, particularly, Abstract). It is concluded that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the grounding means on the inlet line of the flow cell device as taught by Ricchio in the multiple piezoelectric crystal microbalance device of Karube in view of Gardhagen, Thorne, and Takeuchi in order to minimize electronic noise. The advantage of minimizing electronic noise provides the motivation to combine teachings of Karube in view of Gardhagen, Thorne, and Takeuchi and Ricchio et al. with a reasonable expectation of success. Clearly this rejection is based on hindsight reconstruction of the references based on Applicants' specification which is impermissible even under KSR. It is not seen how one of ordinary skill in the art would combine the reference to minimize noise. Where is there any suggestion of this in the prior art?

Karube teaches a multiple piezoelectric crystal microbalance device. This device of Karube includes a connecting station (see annotated Fig. 7 above) for receiving and individually operating array of piezoelectric crystal microbalances (col. 9, lines 12-22). It is noted that these microbalances have different coatings but are not individually removable in accordance with the presently claimed invention. The connecting station of Karube includes a connecting panel having an array of cell connecting receptors (see annotated Fig. 7 above), each cell connecting receptor comprising a receptor connector portion for automatic mating operative engagement with a cell connector portion of a piezoelectric crystal microbalance flow-through cell (Fig. 6) upon plugging the flow through cell into the connecting station. Each receptor connector portion comprises a pair of electric connecting ports (reference elements 63 in Fig. 6) for communication with a power and measurement means (Fig. 16 and col. 5, lines 23-49) for oscillating a piezoelectric crystal (reference element 60 in Fig. 6) carrying electrodes (reference element 62 in Fig. 6 and col. 5, lines 27-30) in a cell compartment (reference element 64 in Fig. 6) of one operatively engaged flow-through cell and for measuring oscillating characteristics of the piezoelectric crystal; and a pair of fluid connecting ports (reference elements 65 in Fig. 6) for communication with flowing means for flowing a solution (col. 5, lines 39-49).

With respect to the limitation of "for communication with flowing means for uninterrupted flowing of a solution (75) and a test solution aliquot (83) to and through the cell compartment," a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The fluid connecting ports of Karube would be expected to provide uninterrupted flowing of a solution and a test solution aliquot through the cell compartment via flowing means. This statement is specifically traversed since there is no reason set forth this expectation.

Although Karube's device includes a connecting station with a pair of fluid connecting ports, the device of Karube differs from the instant claims in that pair of connecting ports provide flow for the plurality of piezoelectric crystal microbalance flow-

through cells instead of having a pair fluid connecting ports associated with each of the receptor connecting portion for individual piezoelectric crystal microbalance flow-through cells. However, Karube differs from the claimed invention in that Karube fails to teach that the plurality of piezoelectric crystal microbalance flow-through cells is individually detachable.

Gardhagen teaches that a piezoelectric determination of analytes using biosensor flow cells (see entire document, particularly, col. 5, lines 15-30). Gardhagen further teaches a multisensory system such as parallel biosensor flow cells be arranged to have an array of flow cells having inlets and outlets (col. 5, lines 32-36).

Thorne teaches a microtitration plates with wells, which are individually removable/detachable (see entire document, particularly, col. 1, lines 19-59). Plates with integrated wells lack versatility (col. 1, lines 19-21). Individually removable wells can be pretreated with different test combinations for different assays. Further, the removable wells enable the tray to be made of a less expensive material than that to the wells, thereby decreasing its expense as compared with those plates with integrated wells.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the device of Karube to have individual flow cells with a pair of fluid connecting ports (inlet and outlet) as taught by Gardhagen in order to allow parallel flow to the plurality of piezoelectric crystal microbalance flow-through cells. The parallel flow configuration is advantageous since the parallel flow configuration allows simultaneous processing of multiple test samples with a reasonable expectation of success. But, where is the teaching of the necessary motivation to combine the references in the expectation of success.

In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the multiple piezoelectric crystal microbalance device of Karube so that the plurality of piezoelectric crystal microbalance flow-through cells are detachable/removable from its base plate holding the array since Thorne teaches that arrays with individually removable wells/reaction cells are advantageous because of their versatility. Further advantage of reducing expense by fabricating the arrays using less expensive material for the base/tray provides further motivation to

combine teaching of Karube in view of Gardhagen and Thorne with a reasonable expectation of success. Again, there is no explanation as to why this would be less expensive than forming the individual cells. This is insufficient reasoning to render prima facie obvious the presently claimed invention.

Further, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the multiple piezoelectric crystal microbalance device of Karube in view of Gardhagen so that the plurality of piezoelectric crystal microbalance flow-through cells are detachable/separable, sine it has been held that constructing a formerly integral structure in various elements involves only routine skill in the art. *In re Dulberg*, 289 F.2d 522, 523, 129 USPQ 348, 349 (CCPA 1961) (The claimed structure, a lipstick holder with a removable cap, was fully met by the prior art except that in the prior art the cap is "press fitted" and therefore not manually removable. The court held that "if it were considered desirable for any reason to obtain access to the end of [the prior art's] holder to which the cap is applied, it would be obvious to make the cap removable for that purpose."). See MPEP §2144.04.

Takeuchi teaches a method of shielding by coating a piezoelectric element with a conductive material such as a metal (see entire document, particularly, col. 17, lines 29-35). A shield layer consisting of a conductive material reduces external electromagnetic noise and improves measurement sensitivity of the piezoelectric element (col. 6, lines 5-9).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include in the multiple piezoelectric crystal microbalance device of Karube in view of Gardhagen and Thorne with a shield layer consisting of a conductive material such as metal as taught by Takeuchi in order to reduce external electromagnetic noise and improve measurement sensitivity of the piezoelectric element. The advantage of reducing external electromagnetic noise provides the motivation to combine teachings of Karube in view of Gardhagen and Thorne and Takeuchi with a reasonable expectation of success as the reduction in

external electromagnetic noise would provide enhanced measurement sensitivity of the piezoelectric element in the multiple piezoelectric crystal microbalance devices.

The rejection of claim 14 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-47 of copending Application No. 10/539,065 in view of Kawakami et al. (USP 5,728,583, Mar. 17, 1998) (hereinafter "Kawakami"), Thorne (USP 4,154,795, May 15, 1979), and constructing a formerly integral structure in various elements involves only routine skill in the art as applied to claim 11 above, and further in view of Ricchio et al. (USP 5,130,095, July 14, 1992) (hereinafter "Ricchio") has been carefully considered but is most respectfully traversed.

The copending application in view of Kawakami and Thorne recites the multiple piezoelectric crystal microbalance devices as set forth above. However, the copending application in view of Kawakami and Thorne fails to recite a multiple piezoelectric crystal microbalance device, further comprising grounding means (108) for electrical grounding of the flow solution (75) and the test solution aliquot (83) to the cell compartment (34) of each of the flow-through cell (10).

Ricchio et al. teaches a flow cell having a solution grounding means on the inlet line for the sample adjacent to the entrance to the flow cell of fluid thereby minimizing electronic noise as set forth above. These reasons fail for the above discussed reason. Moreover, it is noted that this is a provisional rejection and it is requested that this rejection be held in abeyance until there is an allowance of one of the applications.

Applicant's note the Examiner argument that the relationship of the prior art to the claimed invention in the present application are sufficiently similar to those in the *In re Dulberg* decision for it be rendered obviousness of the presently claimed invention is repeated. However, this argument is said not to be found persuasive because Applicant fails to provide specific reasons for stating that the facts with respect to the relationship of the prior art to the claimed invention in the present application are not sufficiently similar to those in the *In re Dulberg* decision. The court has held that constructing a formerly integral structure in various separate elements normally require only ordinary skill in the art and hence are considered routine expedients. As set forth above, Karube differs from the claimed invention in that Karube fails to teach that the plurality of piezoelectric crystal microbalance flow-through cells is detachable. Although

the claimed structure of *In re Dulberg* (lipstick holder with a cap) is different from the currently claimed multiple piezoelectric crystal microbalance device, the facts in *In re Dulberg* the facts are not sufficiently similar due to the complexity of the present invention and that the prior art teachings of Karube in view of Gardhagen does not teach all the elements of multiple piezoelectric crystal microbalance device except that the plurality of piezoelectric crystal microbalance flow-through cells are detachable or separable. Therefore, it is not obvious to one having ordinary skill in the art at the time the invention was made to modify the multiple piezoelectric crystal microbalance device of Kawakami so that the plurality of piezoelectric crystal microbalance flow-through cells are detachable/removable, since it has been held that constructing a formerly integral structure in various/separable elements involves only routine skill in the art. See MPEP §2144.04. Accordingly, it is most respectfully requested that this aspect of the rejection be withdrawn.

In view of the above comments and further amendments to the specification, drawings and claims, favorable reconsideration and allowance of all the claims now present in the application are most respectfully requested.

Respectfully submitted,
BACON & THOMAS, PLLC

By: Richard E. Fichter
Richard E. Fichter
Registration No. 26,382

625 Slaters Lane, Fourth Floor
Alexandria, Virginia 22314
Phone: (703) 683-0500
Facsimile: (703) 683-1080

REF
A05.wpd

March 23, 2009